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Diagnostic Accuracy of Pelvic MRI for Determination of the Cervical Involvement in Endometrial Cancer

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ABSTRACT

Objective: To determine the diagnostic accuracy of pelvic MRI for assessment of the cervical involvement in endometrial cancer.

Study Design: Cross-sectional analytical study.

Place and Duration of Study: Radiology Department of the Aga Khan University Hospital, Karachi from January 2014 to December 2015.

Methodology: Patients with biopsy-proven endometrial cancer were included, who had both their MRI and histopathological diagnosis performed at our institution. Those patients treated with chemo/radiotherapy or had incomplete medical records, were excluded. The extent of cervical involvement by endometrial carcinoma was seen on T2WI images, and findings were correlated after surgery taking histopathology as the gold standard. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy were calculated.

Results: The mean age of the 56 patients was 60.87 ±8.80 years (range 37-84 years). The most common clinical indication was post-menopausal bleeding (n=37, 66.1%). The most common histological subtype was endometrioid adenocarcinoma (n=50, 89.3%). The sensitivity, specificity, diagnostic accuracy, positive and negative predictive values of MRI in the detection of cervical invasion were 92.85%, 88.09%, 89.28%, 72.22% and 97.36%, respectively.

Conclusion: MRI is a highly sensitive and specific imaging modality for detection of cervical invasion in endometrial carcinoma.

Key Words: *Endometrial carcinoma. Cervical involvement. Magnetic resonance imaging. Diagnostic accuracy.*

INTRODUCTION

The most common gynecological malignancy and the fourth most common cancer of female in the United States is endometrial carcinoma.¹ Internationally, it makes up 6% of all cancers in females.² It has an incidence of 5.9 per 100,000 women in developing countries, and the second most common gynecological malignancy. Endometrial cancer is diagnosed mainly during the 6th and 7th decades.³ The 10-year survival rate is 75%, because 75-80% of women present with symptoms of postmenopausal bleeding at an early stage.⁴

The risk factors associated with the development of endometrial cancer include obesity, nulliparity unopposed estrogen intake, Stein-Leventhal syndrome, diabetes mellitus, Lynch syndrome, and tamoxifen therapy.⁵ Diagnosis, however, is done with either hysteroscopic-guided endometrial biopsy or dilation and curettage.

Histologically, there are two subtypes of endometrial cancer.⁶ The most frequent is endometrioid adenocarcinoma (Type I) which is 90% of all endometrial

tumors.³ In Pakistan, adenocarcinoma is the most common histological type accounting for 85.8%.^{7,8} Endometrial cancer frequently occurs in a background of endometrial hyperplasia, which is common in the beginning of menopause, are usually low grade, and show a good prognosis.⁹ Type II endometrial cancers include all other histological subtypes namely clear-cell, serous papillary and carcinosarcomas. Type II cancers often occur in elderly females, show no relationship with increased levels of estrogen or atypical hyperplasia, have a poorer prognosis, and spread like ovarian cancer.¹⁰

In 1988, surgicopathologic International Federation of Gynecology and Obstetrics (FIGO) devised staging for endometrial cancer.¹¹ In 2009, few specific changes were made in staging.^{12,13} In the new staging system, stage I was further divided into two substages: Ia (showing equal/less than 50% myometrial invasion), and Ib (showing equal/greater than 50% myometrial invasion), in contrast with the older system, which had three sub-stages; Ia (confined to endometrium), Ib (showing less than 50% myometrial invasion), and Ic (showing equal/greater than 50% myometrial invasion). There are no sub-stages for stage II, and only cervical stromal involvement (stage IIb, old system) is considered and endo-cervical glandular invasion (stage IIa, old system) is now diagnosed as stage I endometrial cancer.¹¹

Accurate staging of endometrial cancer is crucial at the time of diagnosis to successfully manage patients and

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thus increase survival rate.¹¹ A study conducted by Taufiq *et al.* reported a potential role of MRI for determining myometrial invasion.¹⁴ The data about the role of Magnetic Resonance Imaging (MRI) in staging of endometrial cancer, particularly in detection of cervical invasion in our country, is limited.

The aim of this study was to determine the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of MRI in the detection of cervical involvement by endometrial carcinoma.

METHODOLOGY

It was a cross-sectional analytical study conducted at the Department of Radiology, The Aga Khan University Hospital (AKUH), Karachi, Pakistan from January 2014 to December 2015. Exemption was taken for this retrospective study from Ethical Review Committee of the Hospital. The sample size was calculated using the Lin Naing sample size calculator. The sensitivity and specificity of MRI T2 weighted images (T2WI) for determination of cervical invasion has been calculated to be 100% and 95%, respectively; the reported prevalence of endometrial cancer is 6%. Therefore with a confidence interval of 95%, and a 6% error margin, the calculated sample size was 56 patients. Purposive non-probability sampling was applied. The inclusion criteria were all patients (all ages) with histology proven endometrial carcinoma on biopsy, and had their MRI pelvis for staging before hysterectomy, who then underwent surgery and histopathology at our hospital. All patients treated with radiotherapy/chemotherapy or patients with incomplete medical records were excluded. The final histological diagnoses, i.e. invasion of cervix and final staging of patients, was recorded.

Imaging protocol included all routine sequences comprising coronal T1W, axial, sagittal, coronal T2W, axial T1W fat suppressed, and sagittal T1W post-contrast with fat suppression images. T2W imaging was done by the protocol set in our department for female pelvis, with the following parameters: TR/TE 3900/76; field of view 38 cm; slice thickness 4 mm; gap 0; number of excitations 4; matrix 192x192; 3 acquisitions with 8 slices per acquisitions; and phase encoding direction, anterior to posterior. The time needed to obtain the T2W images was set to 4 minutes.

Scan reading was performed by two independent radiologists with greater than 5 years of experience in women imaging. MRI results were compared with final histopathology setting letter as gold standard. True positive was taken if abnormal signal of endometrium, i.e. hyperintense to myometrium and hypointense to normal endometrium, was seen extending into cervix on T2WI, and cervical invasion was reported on histopathology. True negative was taken if abnormal

signal of endometrium, i.e hyperintense to myometrium and hypointense to endometrium, was not extending into cervix and invasion of cervix not seen on histopathology.

Statistical analysis was performed on SPSS (version 21.0). Mean and standard deviation were calculated for all continuous variables and frequencies with percentages were calculated for categorical ones.

Sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and accuracy were determined. Positive cases comprised true positives and false negatives; and negative cases comprised true negatives and false positives.

RESULTS

Fifty-six patients had a mean age of 60.87 ± 8.80 years (range 37-84 years). The most common clinical indication was post-menopausal bleeding ($n=37$, 66.1%) followed by increased endometrial thickness on ultrasound ($n=11$, 19.6%) and irregular vaginal bleeding in pre-menopausal patients ($n=4$, 7.1%). The most common histological subtype was the endometrioid adenocarcinoma detected in 89.3% ($n=50$) of the patients.

In MRI on T2W images, endometrial carcinoma appeared heterogeneous in 23 patients (Figure 1, 41.1%); hypointense in 24 patients (42.9%); and hyperintense in nine patients (16.1%). On diffusion weighted images (DWI), 52 patients (92.9%) showed diffusion restriction and four patients (7.1%) were negative for diffusion restriction. On T1W fat sat post contrast images, 26 cases (46.4%) did not show enhancement, 25 cases (44.6%) showed mild enhancement, and five cases (8.9%) showed heterogeneous enhancement. On T2W images, cervical involvement was detected in 18 patients (32.1%); while in 38 patients (67.9%), cervical involvement was not detected.

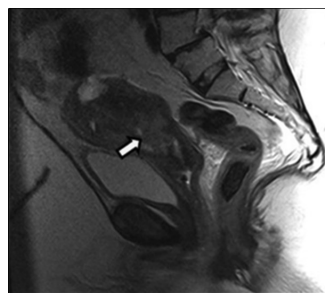


Figure 1: T2 weighted image demonstrating anteverted uterus showing neoplastic mass (arrow) involving the endometrium and the cervix.



Figure 2: T2 weighted image demonstrating anteverted uterus showing neoplastic mass (arrow) involving the endometrium extending up to the cervix.

On histopathology report, cervical involvement was detected in 15 patients (26.8%); while in 41 patients (73.2%), cervical involvement was not detected. A total of 13 out of 18 patients (72.2%), who showed cervical invasion on the T2W MRI (Figure 2), turned out to be positive on histopathology (true positive) and 5 out of 18

Table I: Accuracy of pelvic MRI for assessment of the cervical involvement in endometrial cancer.

T2W MRI cervical invasion	Histopathology cervical invasion		
	Positive	Negative	Total
Positive	13	05	18
Negative	01	37	38
Total	14	42	56

TP=True-positive, n=13; FP=False-positive, n=05; FN=False-negative, n=01; TN=True-negative, n=37.
Sensitivity=92.85%, Specificity=88.09%, PPV=72.22%, NPV=97.36%, Accuracy=89.28%.

patients (27.7%) who showed cervical invasion on T2W MRI, were negative on histopathology (false positive).

Out of 38 patients, 37 (97.3%) did not show cervical invasion on MRI, were negative for cervical invasion on histopathology (true negative); while one out of these 38 patients (2.63%) who were negative on MRI for cervical invasion came out to be positive for cervical invasion on histopathology (false negative).

In evaluation of cervical infiltration, the sensitivity, specificity, positive, negative predictive and diagnostic accuracy, values of T2W MRI with 95% confidence interval were 92.85%, 88.09%, 72.22%, 97.36% and 89.28%, respectively (Table I).

DISCUSSION

There are various imaging modalities such as ultrasound and computed tomography (CT) scan available for the assessment of endometrial carcinoma but MRI gives far more information with regard to its extent which helps in treatment planning and determining prognosis.

Transvaginal ultrasound (TVUS) is a rapid, low-cost, non-ionizing modality often used as a first imaging in initial workup of women with complaint of post-menopausal bleeding.³ Endometrial carcinoma is typically visualised as thickening of the endometrial lining, and TVUS is used to measure this thickened endometrial lining in the antero-posterior diameter, to reach a diagnosis. The sensitivity and specificity of TVUS for detecting endometrial carcinoma approach 96% and 61%, respectively, when endometrial thickness of 5 mm, in postmenopausal women, is used to define abnormal endometrial thickening.¹³ But it is hard to demarcate the tumor margins on TVUS, particularly when the tumor is diffusely infiltrating the myometrium.¹⁵ Drawbacks of TVUS are that it is highly operator-dependent, and has limited field of view. It may overestimate myometrial invasion when the tumor is large, or patient has adenomyosis, and lymphovascular invasion. Additionally, there is inadequate information about the role of TVUS in delineating cervical invasion, parametrial extension, or lymph node involvement.¹⁶

On contrast enhanced Computed Tomography, endometrial carcinoma is seen as a hypodence and less enhancing area within the endometrial cavity. This appearance is not specific enough, thus differential

diagnoses such as sub-mucosal leiomyomas, endometrial polyps etc. cannot be fully excluded.³ CT shows less sensitivity and specificity in correctly determining myometrial involvement and cervical invasion as opposed to MRI. Therefore, it appears to have a limited role in local staging due to its suboptimal soft tissue delineation. The sensitivity and specificity of CT in determining myometrial involvement ranges from 40% to 83% and 42% to 75%, respectively.¹⁷ Recent studies done to assess preoperatively, the myometrial and cervical extension of endometrial carcinoma with multi-detector CT showed better diagnostic accuracy of 95% and 81%, respectively.¹⁸ At present, CT is used generally in the assessment of advanced stage disease, i.e. for evaluating patients with endometrial carcinoma by determining nodal and distant metastases.

MRI achieves the greatest accuracy, for pre-treatment local staging of endometrial cancer, mainly due to its superb soft tissue delineation. On MRI, endometrial carcinoma is usually detected as a hypo-to-isointense mass on T1WI, showing intermediate signal intensity less than the normal endometrium on T2WI.³ On post-contrast dynamic imaging, endometrial carcinoma enhances a lesser amount than the myometrium. On the whole, staging accuracy of MRI is reported to be 83-92%.^{19,20}

The usual signal of normal cervical stroma on T2WI is low, this becomes distinct to the high-intermediate signal intensity of tumor infiltration.²¹ The sensitivity, specificity, and diagnostic accuracy of MR in determination of cervical infiltration have been reported to be 100%, 87%, and 90%, respectively and on T2WI 100%, 95%, and 96%, respectively.²²

In this study, most of the patients were post-menopausal and presented with post-menopausal bleeding. Endometrial carcinoma was detected on T2WI, DWI as well as on T1W fat sat post contrast images but cervical invasion was best detected on T2W images with diagnostic accuracy approaching 89.28%.

In a study conducted by Zamani *et al.*, the sensitivity and specificity in cervical stromal infiltration was higher in distinction to mucosal infiltration, 54.54% and 100% vs. 71.4% and 97.5%, respectively.¹¹

In another study conducted by Seki *et al.*, the overall accuracy of MRI in predicting cervical infiltration was determined to be 90-92%, with sensitivity of 75-80% and specificity of 94-96%.²³

This study shows the sensitivity and specificity for cervical stromal involvement as 92.85% and 88.09%, respectively. The sensitivity of this study was higher than studies conducted by Zamani *et al.* and Seki *et al.* probably because of the larger sample size.

MRI's greater soft tissue delineation allows it to be a superior than other cross-sectional imaging modalities in determining adnexal metastases, invasion of vagina,

urinary bladder, and rectum. It is thought that with the new 2009 FIGO staging system, an improved accuracy in MRI staging is obtained.^{24,25}

The main limitation of this study was the inter-observer agreement between the two consultants, which was not taken into account. Furthermore, the patients who underwent curettage before MRI were not excluded from this study; thus the imaging performed after cervical curettage may result in abnormal signal intensity, replacing the normal hypointense signal intensity of cervix.

CONCLUSION

At present, MRI is an accurate, sensitive and specific modality for cervical invasion of endometrial carcinoma.

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